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Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Published online: 12 Mar 2010.

To cite this article: Sumit V. Jadhav , Pravin G. Ingole & Hari C. Bajaj (2010) Ionic-Liquid Salt-Mediated Synthesis of 4′-(Pyridyl)-terpyridines, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 40:8, 1142-1148, DOI: 10.1080/00397910903046838

To link to this article: http://dx.doi.org/10.1080/00397910903046838

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Synthetic Communications®, 40: 1142–1148, 2010
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ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910903046838

IONIC-LIQUID SALT-MEDIATED SYNTHESIS OF 4′-(PYRIDYL)-TERPYRIDINES

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One-pot reactions to produce isomeric 4′-(pyridyl) 2,2′:6′,2″-terpyridine under moderate conditions are described using imidazolium-based ionic liquid and quaternary ammonium-based molten salts as solvent media. The use of eutectic molten salts as a reaction media proved effective in sequential aldol and Michael addition reactions, leading to substituted terpyridines. The desired product was obtained in reasonable yield via a simple, one-pot reaction.

Keywords: Green chemistry; ionic liquid; quaternary ammonium salts; terpyridines

INTRODUCTION

Over the past couple of years, the oligopyridines and in particular 2,2′:6′,2″-terpyridines (TPY) have been the subject of intensive investigation in the area of supramolecular chemistry. Organic moieties bearing TPY subunits are extremely versatile building blocks for the construction of libraries of metallo-supramolecular assemblies as a consequence of their favorable geometry, which leads to coordination with various metal ions.[1,2] The enormous interest in this class of compounds has been driven by their strong metal-to-ligand charge-transfer transitions, facile electron-transfer properties, and sufficiently extendable ^{3}MLCT (metal-to-ligand charge transfer) excited states.[3] In recent times, TPYs have drawn wide attention because of their potential applications in photochemistry for the design of luminescent devices or as sensitizers for light-to-electricity conversion[4] and dye-sensitized solar cells,[5] in catalysis,[6] in nanoscience,[7,8] and in biochemistry.[9–11]

For the diverse range of applications, easy access to differently functionalized TPY on a large scale and good yields are prerequisites. Conventional approaches to TPY synthesis involves either coupling reactions of pyridine subunits,[12,13] condensation reactions,[14,15] or pyrolysis[16]; however, these methods suffer several disadvantages such as multistep procedure, long reaction time, poor yield, and use of

Received February 1, 2009.

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volatile organic compounds (VOCs) and toxic reagents. As a consequence, for the stringent and growing environmental regulations, it is desirable to develop environmentally cautious synthetic methods with minimal toxics, a foremost requirement of green chemistry.[17] To date, polyethylene glycol (PEG)-mediated synthesis of TPY via 1,5-diketone intermediate, reported by Smith et al.[18] is the most prominent approach to synthesis of the target compound, both in the context of generality and simplicity of the procedure. As we find in the literature, the various molten-salt systems were successfully investigated as solvent media.[19,20] To the best of our knowledge, synthesis of TPY in such solvent media has rarely been reported.

Herein, we have reported facile and clean synthesis of a series of isomeric 4′-(pyridyl)-terpyridines **1–6** from appropriate precursors using imidazolium-based ionic liquid (IL) as well as quaternary ammonium sulfates as reaction media.

EXPERIMENTAL

Materials

Isomeric pyridine carboxyaldehydes, acetyl pyridines, and imidazolium-based ILs were purchased from Sigma-Aldrich (USA). Quaternary ammonium salts were synthesized from n-propyl amine and di-ethylenetriamine, obtained from Spectrochem Fine Chemicals, Ltd. (India). Other common solvents and reagents were obtained from S.D. Fine Chemicals, Ltd. (India). All chemicals were used as received without further purification.

General

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AX500 spectrometer using $CDCl_3$ as solvent and tetramethylsilane as an internal reference. Gas chromatography–mass spectrometry (GC-MS) analyses were performed on a Shimadzu QP-2010 spectrometer. Elemental analyses were done on a Perkin-Elmer 2400 CHNS/O analyzer.

Synthesis of Quaternary Ammonium Salts

Quaternary ammonium salts were synthesized by the procedure reported elsewhere.[21] Sulfuric acid (0.1 mol) was added to 0.1 mol corresponding amine taken in 50 ml chloroform in a 100-ml round-bottom flask under vigorous stirring. The temperature was kept at 0 °C. After the reaction, chloroform was removed using a rotary evaporator. The crystalline solids obtained were further dried by evaporation under high vacuum at 60 °C.

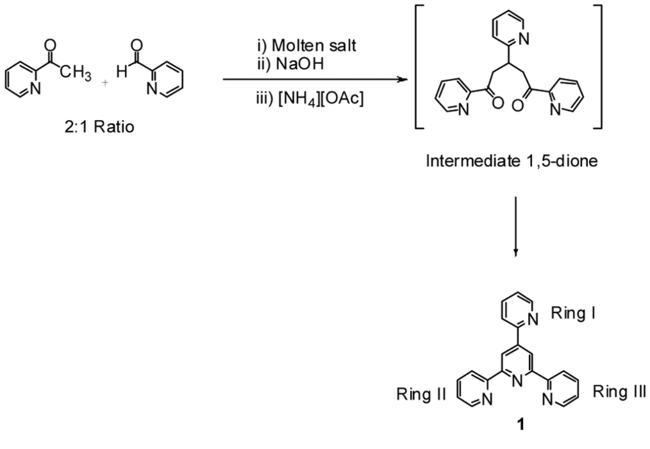
Synthesis of 4′-(Pyridyl)-terpyridines

In a typical reaction, 2-acetylpyridine (2.42 g, 20 mmol), was added to a suspension of 1-butyl-3-methylimidazolium tetrafluoroborate (10 cm^3) crushed with sodium hydroxide (0.8 g, 20 mmol) in a 100-ml round-bottom flask, and the mixture was stirred for 10 min under ice. 2-Pyridine carboxyaldehyde (1.07 g, 10 mmol) was then added, and the suspension was kept at 0 °C for 2 h, with frequent manual stirring. During this time, the reaction mixture turned wine red. After 2 h, ammonium acetate (10 g, excess) was added, and the mixture was refluxed at 110 °C for 2 h to yield a dark-brown semi-crystalline precipitate. Cold water was then added to facilitate the precipitation of product. Precipitate of **1** was isolated by filtration using a suction filter pump, washed with 20 ml × 2 methanol–water mixture (1:5), and recrystallized in chloroform (method 1). The product formed was characterized by ^{1}H and ^{13}C NMR spectroscopy. Light yellow solid; yield 1.62 g (52%).

In the case of quaternary ammonium salts, a single-step process was adapted (method 2) in which all the reagents were added simultaneously along with quaternary ammonium salts (4 g) instead of 1-butyl-3-methylimidazolium tetrafluoroborate. Although quaternary ammonium salts are solid at ambient temperature, upon mixing with ammonium acetate, a sticky eutectic mixture is formed, which promotes the reaction much faster. All other reagents were added in the same stoichiometric quantity as in method 1, and the resulting mixture was directly refluxed at 140 °C for 4 h; further workup was the same as in method 1.

RESULTS AND DISCUSSION

Incorporation of pyridyl functionalities into the 4′-position of the 2, 2′:6′,2″-terpyridine in two steps as well as a single reaction step is demonstrated. Treatment of 2-acetylpyridine and 2-pyridine carboxyaldehyde (2:l ratio) with ammonium acetate in imidazolium-based IL as reaction medium afforded the target product **1** in good yield in a two-step reaction (Scheme 1), whereas the eutectic mixture of quaternary ammonium salts with ammonium acetate yields the title compounds in a single step. The reaction is believed to proceed through a 1,5-diketone intermediate [21] that can be readily converted into product **1**. Both the methods to synthesize TPY in the molten salts are simple and easy to use. These solvent systems are becoming benign and are alternative reaction media in synthetic chemistry.



Scheme 1. Synthesis of TPY using molten salts as solvent media.

Table 1. Yields and elemental analysis of synthesized 4′-(pyridyl)-terpyridines

			Yield (%)[a]			Elemental analysis experimentally found (%)[b]		
Compound	Ring I	Rings II, III	IL 1	Salt 1	Salt 2	C	H	N
1	2-Pyridyl	2-Pyridyl	52	48	49	77.1	4.4	17.9
2	3-Pyridyl	2-Pyridyl	42	35	35	77.7	4.6	18.3
3	4-Pyridyl	2-Pyridyl	46	38	36	77.6	4.7	18.3
4	2-Pyridyl	3-Pyridyl	41	40	40	77.5	4.3	18.1
5	3-Pyridyl	3-Pyridyl	46	40	44	77.3	4.6	18.3
6	4-Pyridyl	3-Pyridyl	45	38	42	77.6	4.1	17.9

[a] IL 1, 1-butyl 3-methyl imidazolium tetrafluoroborate; salt 1, di-ethylenetriamine sulfate; salt 2, n-propylamine sulfate.

[b] Theoretically calculated elemental analysis results are C = 77.4%, H = 4.55%, and N = 18.05%.

Eutectic molten salts have many fascinating properties, including no measurable vapor pressure (hence cannot emit VOCs), nonflammability, high polarity, and solubility for a wide range of materials including inorganic, organic, and even polymeric materials. Molten salts (ILs) can be broadly categorized as imidazolium-based and quaternary ammonium salts.

To optimize the reaction temperature in method 2, the reaction of 2-acetylpyridine, 2-pyridine-carboxyaldehyde, and ammonium acetate with NaOH was carried out at temperatures ranging from 100 to 140 °C in increments of 10 °C. The better yields were obtained at 140 °C and remain unaffected when temperature was further increased to 160 °C. Under these optimized reaction conditions (140 °C), we have synthesized a series of six isomeric 4′-(pyridyl)-terpyridines **1**–**6** in acceptable purity and yields using method 1 with imidazolium-based IL and method 2 with quaternary ammonium salts (Table 1). Being hydrophilic, salts can be removed easily from the product by extensive washing with water. The product **1** in purified form can easily be collected by filtration instead of tedious column chromatography, which reduces the VOCs.

Although cleaner reaction conditions leading to good yields and purity are observed in imidazolium-based solvents via method 1, the high cost remains a main hurdle to employing these ecofriendly solvents on a pilot scale. There is a need for alternative reaction media that can satisfy expectations regarding yield and purity of the compounds. In present work, we have synthesized and used two quaternary ammonium salts (n-propylamine sulfate and di-ethylenetriamine sulfate) as nontoxic and nonvolatile reaction media, which are emerging as ideal candidates in a variety of synthetic organic transformation because of their ease of preparation and in particular low cost. They gave comparable yield of the products with already existing methods[21] (i.e., in PEG, about 44–55%).

The compounds are characterized by ^{1}H and ^{13}C NMR spectroscopy.

Spectral Data

Compound 1. Yellow powder, δ_H (500 MHz, $CDCl_3$) 9.09 (s, 2H, Ar), 8.80 (m, 1H, Ar), 8.74 (m, 2H, Ar), 8.66 (d, 2H, Ar), 8.10 (d, 1H, Ar), 7.87 (dt, 2H, Ar), 7.85 (dt, 1H, Ar), 7.35 (m, 3H, Ar). δ_C (125 MHz, $CDCl_3$) 156.21, 156.14, 155.05, 150.02, 149.19, 148.61, 136.90, 136.87, 123.86, 123.75, 121.33, 121.29, 118.61. GC-MS (EI): *m*/*z* (%) 310 (100) $[M]^+$.

Compound 2. Light brown solid, δ_H (500 MHz, $CDCl_3$) 9.13 (dd, 1H, Ar), 8.73 (s, 2H, Ar), 8.70 (m, 2H, Ar), 8.66 (dd, 1H, Ar), 8.57 (m, 2H, Ar), 8.20 (m, 1H, Ar), 7.89 (dt, 2H, Ar), 7.48 (m, 1H, Ar), 7.37 (m, 2H, Ar). δ_C(125 MHz, $CDCl_3$) 156.23, 155.85, 150.10, 149.19, 148.43, 147.22, 136.96, 134.69, 134.27, 124.06, 123.67, 121.39, 118.80. GC-MS (EI): *m*/*z* (%) 310 (100) $[M]^+$.

Compound 3. Mauve solid, δ_H (500 MHz, $CDCl_3$) 8.89 (s, 2H, Ar), 8.84 (m, 2H, Ar), 8.75 (dd, 2H, Ar), 8.65 (d, 2H, Ar), 7.97 (dt, 2H, Ar), 7.53 (m, 2H, Ar), 7.41 (dd, 2H, Ar). δ_C (125 MHz, $CDCl_3$) 156.41, 155.73, 150.57, 149.24, 149.22, 145.58, 137.01, 124.15, 121.72, 121.39, 118.67. GC-MS (EI): *m*/*z* (%) 310 (100) $[M]^+$.

Compound 4. White solid, δ_H (500 MHz, $CDCl_3$) 9.56 (m, 2H, Ar), 8.82 (m, 1H, Ar), 8.72 (dd, 2H, Ar), 8.70 (dt, 2H, Ar), 8.57 (s, 2H, Ar), 7.97 (d, 1H, Ar), 7.90 (dt, 1H, Ar), 7.50 (dd, 2H, Ar), 7.44 (m, 1H, Ar). δ_C (125 MHz, $CDCl_3$) 155.57, 154.42, 150.26, 150.19, 148.56, 148.49, 137.31, 134.59, 134.57, 124.23, 123.63, 121.10, 117.08. GC-MS (EI): *m*/*z* (%) 310 (100) $[M]^+$.

Compound 5. White powder, δ_H (500 MHz, $CDCl_3$) 9.39 (m, 2H, Ar), 9.02 (m, 1H, Ar), 8.74 (dd, 1H, Ar), 8.72 (dd, 2H, Ar), 8.54 (dt, 2H, Ar), 8.08 (dt, 1H, Ar), 7.96 (s, 2H, Ar), 7.52 (dd, 1H, Ar), 7.49 (dd, 2H, Ar). δ_C (125 MHz, $CDCl_3$) 155.78, 150.54, 150.45, 148.40, 148.22, 147.46, 134.66, 134.61, 134.39, 134.33, 124.04, 123.73, 117.61. GC-MS (EI): *m*/*z* (%) 310 (100) $[M]^+$.

Compound 6. Light brown solid, δ_H (500 MHz, $CDCl_3$) 9.48 (m, 2H, Ar), 8.87 (m, 2H, Ar), 8.73 (dd, 2H, Ar), 8.54 (dt, 2H, Ar), 7.97 (s, 2H, Ar), 7.67 (m, 2H, Ar), 7.52 (dd, 2H, Ar). δ_C (125 MHz, $CDCl_3$) 155.92, 150.88, 150.57, 148.45, 148.42, 145.65, 134.57, 134.21, 123.73, 121.60, 117.42. GC-MS (EI): *m*/*z* (%) 310 (100) $[M]^+$.

CONCLUSION

A novel, convenient route for the introduction of pyridyl ring in the 4′-position of the terpyridine using nontoxic solvent systems has been established. Besides ([BMIM] [BF_4]), some eutectic mixtures of quaternary ammonium molten salts were employed, which were relatively cheap and easy to prepare. Yield of the products comparable with already existing methods (i.e., in PEG about 44–55%: see Ref. 21), accessible starting materials, and relative ease of workup are sufficient advantages to open a new avenue in the synthesis of terpyridines using less hazardous conditions.

ACKNOWLEDGMENTS

We gratefully acknowledge the Council of Scientific and Industrial Research, New Delhi, India, for funding under the network project NWP-0010. We also thank the Analytical Sciences Discipline of the institute for analysis facilities.

REFERENCES

1. Hofmeier, H.; Schubert, U. S. Recent developments in the supramolecular chemistry of terpyridine–metal complexes. *Chem. Soc. Rev.* **2004**, *33*, 373–399.
2. Kaes, C.; Katz, A.; Hosseini, M. Bipyridine: The most widely used ligand: A review of molecules comprising at least two 2,2′-bipyridine units. *Chem. Rev.* **2000**, *100*, 3553–3590.
3. Medlycott, E. A.; Hanan, G. S. Designing tridentate ligands for ruthenium(II) complexes with prolonged room temperature luminescence lifetimes. *Chem. Soc. Rev.* **2005**, *34*, 133–142.
4. Kohle, O.; Ruike, S.; Gratzel, M. Ruthenium(II) charge-transfer sensitizers containing 4,4′-dicarboxy-2,2′-bipyridine: Synthesis, properties, and bonding mode of coordinated thio- and selenocyanates. *Inorg. Chem.* **1996**, *35*, 4779–4787.
5. O'Regan, B.; Moser, J.; Anderson, M. A.; Gratzel, M. Vectorial electron injection into transparent semiconductor membranes and electric field effects on the dynamics of light-induced charge separation. *J. Phys. Chem.* **1990**, *94*, 8720–8726.
6. Yoo, D. W.; Yoo, S. K.; Kim, C.; Lee, J. K. A novel mononuclear Fe(III) mono(terpyridine) complex having labile solvent ligands and its catalytic activity. *J. Chem. Soc., Dalton Trans.* **2002**, *21*, 3931–3932.
7. Umeda, K.; Nakamura, A.; Toda, F. Calatytic mechanism and activity of bis(2,2′:6′,2″-terpyridine) rhodium(III) for the reduction of NAD^+ into NADH in a photosensitized reaction system. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2260–2267.
8. Ziener, U.; Lehn, J. M.; Mourran, A.; Möller, M. Supramolecular assemblies of a bis(terpyridine) ligand and of its $[2 \times 2]$ grid-type Zn^{II} and Co^{II} complexes on highly ordered pyrolytic graphite. *Chem. Eur. J.* **2002**, *8*, 951–957.
9. Zak, B.; Baginsky, E. S.; Epstein, E.; Weiner, L. M. Terosite sulfonate: A sensitive reagent for the determination of serum iron. *Clin. Chim. Acta* **1970**, *29*, 77–82.
10. Carter, P. J.; Cheng, C. C.; Thorp, H. H. J. Oxidation of DNA and RNA by oxoruthenium(IV) metallointercalators: Visualizing the recognition properties of dipyridophenazine by high-resolution electrophoresis. *J. Am. Chem. Soc.* **1998**, *120*, 632–642.
11. Zhang, Y.; Murphy, C. B.; Jones, W. E. Poly[*p*-(phenyleneethynylene)-*alt*-(thienyleneethynylene)] polymers with oligopyridine pendant groups: Highly sensitive chemosensors for transition metal ions. *Macromolecules* **2002**, *35*, 630–636.
12. Schubert, U. S.; Eschbaumer, C.; Weidl, C. H. Synthesis of 5,5″-*bis*-functionalized 2,2′:6′,2″-terpyridines using functionalized pyridine building blocks. *Synlett* **1999**, *3*, 342–344.
13. Cardenas, D. J.; Sauvage, J. P. Improved synthesis of 2, 6-oligopyridines by Stille cross-coupling reaction. *Synlett* **1996**, *9*, 916–918.
14. Thummel, R. P. The application of Friedländer and Fischer methodologies to the synthesis of organized polyaza cavities. *Synlett* **1992**, *1*, 1–12.
15. Thummel, R. P. The synthesis and properties of organized polyaza cavity-shaped molecules. *Tetrahedron* **1991**, *47*, 6851–6886.
16. Bell, T. W.; Firestone, A. Construction of a soluble heptacyclic terpyridine. *J. Org. Chem.* **1986**, *51*, 764–765.
17. Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, UK, 1998.
18. Smith, C. B.; Raston, C. L.; Sobolev, A. N. Poly(ethyleneglycol)(PEG): A versatile reaction medium in gaining access to 4′-(pyridyl)-terpyridines. *Green Chem.* **2005**, *7*, 650–654.
19. Jones, S. D.; Blomgren, G. E. Low-temperature molten salt electrolytes based on aralkyl quaternary or ternary onium salts. *J. Electrochem. Soc.* **1989**, *136*, 424–427.

20. Liao, J. H.; Wu, P. C.; Bai, Y. H. Eutectic mixture of choline chloride/urea as a green solvent in synthesis of a coordination polymer: $[Zn(O_3PCH_2CO_2)] \cdot NH_4$. *Inorg. Chem. Commun.* **2005**, *8*, 390–392.
21. Weng, J.; Wang, C.; Li, H.; Wang, Y. Novel quaternary ammonium ionic liquids and their use as dual solvent–catalysts in the hydrolytic reaction. *Green Chem.* **2006**, *8*, 96–99.